

**REMARKS**

**A. Status of the Claims**

By the present amendment, claims 67, 91, 111, and 129 have been amended to more particularly define the Applicant's invention and to claim it with greater specificity. Claims 146-180 have been canceled. Claims amendments are supported by the specification and the original claims. No new matter has been added.

The Applicant has noticed that the Office Action indicates that claim 110 stands objected to by the Examiner (see, the summary page, item 7). The Office Action does not mention any rejection of this claim. The Applicant has been unable to determine what the grounds for these objections are, and the text of the Office Action does not provide any explanation. Accordingly, the Applicant requests clarification as to the grounds of objection to claim 110 to enable the Applicant to respond to the objections.

After the proposed amendment has been entered, claims 67, 70, 73-81, 84-91, and 95-145 will be pending and under consideration.

**B. Rejections Under 35 U.S.C. § 102 (e)**

Claims 67, 70, 73-81, 84-89, 91, 96-108, 111-127, 129, 131-143, 146-162, 164, and 166-178 stand rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by U.S. Patent No. 5,981,601 to Nagley et al. ("Nagley") (page 4, lines 10-13 of the Office Action). The rejection is respectfully traversed.

The standard that a reference must meet to be validly used as a basis for a rejection of a claim by anticipation was discussed in a response to a previous Office Action. It is submitted that Nagley does not meet this standard as it fails to describe all the elements and limitations recited in each of claims 67, 91, 111, and 129.

Indeed, each of the instant claims 67 and 91 recites a method of treatment or for reducing or eliminating symptoms of one of the following diseases or disorders: of mitochondrial renal tubular acidosis, multiple mitochondrial deletion syndrome, Leigh syndrome, lactic acidemia, 3-hydroxybutyric acidemia, 1+proteinuria, pyruvate dehydrogenase deficiency, complex I deficiency, complex IV deficiency, aminoaciduria, hydroxyprolinuria, and MARIAHS syndrome. Please note that by the present amendment the methods directed to the treatment of encephalomyopathy have been deleted from each of the instant claims 67 and 91.

Nagley teaches methods for the treatment of only the following diseases: Lebers disease, hereditary optic neuropathy, encephalomyopathy lactic acidosis, stroke-like episodes, chronic progressive external ophthalmoplegia, Kearns-Sayre syndrome, Pearson's marrow/pancreas syndrome, various cardiomyopathies, Parkinson's Disease, Alzheimer's Disease as well as heart failure, stroke and diabetes (see, col. 8, line 65 through col. 9, line 8). As one can clearly see from a simple comparison, Nagley fails to explicitly teach or inherently describe any of the specific diseases recited in claims 67 and 91, as amended. To state it succinctly, the instant claims 67 and 91 are directed to the treatment of the diseases and disorders that are different from those that can be treated according to the teachings of Nagley.

Turning now to claims 111 and 129, each of these claims is directed to the methods that consist only of administering a composition having only one active compound, such as a compound of Formula (I) or (IA). The Applicant is aware that the Examiner has fully appreciated the meaning of the transitional clause "consisting of" used in claims 111 and 129 that excludes the use of any other active compounds.

The Examiner, however, pointed out (see, page 4, lines 14-17 of the Office Action) that the process of administering of the composition was open to additional steps that may include administration of an additional compound, such as a redox compound such as a benzoquinone derivative found in Nagley. Accordingly, each of the instant

claims 111 and 129 has been amended and the language of these claims has been adjusted to recite “the method consisting of administering” the above-described composition that includes a single active compound.

As previously discussed, Nagley fails to disclose or suggest using a composition having a single active compound, and requires using a minimum of two active compounds. Therefore, Nagley cannot be used for the rejection by anticipation.

In sum, Nagley fails to disclose every element of claims 67, 91, 111, or 129, as amended, and, therefore, is not a proper prior art reference under 35 U.S.C. § 102(e). Thus, each of claims 67, 91, 111, or 129 is patentably distinguishable over Nagley. Each of claims 70, 73-81, 84-89, 91, 96-108, 111-127, 129, 131-143 directly or indirectly depends on either claim 67, 91, 111, or 129, and is accordingly considered patentable for at least the same reason. As to claims 146-162, 164, and 166-178, the rejection has become moot in view of the cancellation of claims 146-180. Withdrawal of the rejection and reconsideration are respectfully requested.

**C. Rejections Under 35 U.S.C. § 103 (a)**

Claims 67, 70, 73-81, 84-91, 96-109, and 111-179 stand rejected under 35 U.S.C. § 103(a) as allegedly being obvious Nagley in view of Page et al., “Developmental Disorder Associated with Increased Cellular Nucleotidase Activity,” *Proc. Natl. Acad. Sci. USA*, vol. 94, pp. 11601-11606 (1997) (“Page”)(page 4, last paragraph of the Office Action). The rejection is respectfully traversed.

The *KSR* standard that has to be satisfied in order to make a valid rejection based on a prima facie case of obviousness was described in a response to a previous Office Action. It is submitted that this standard has not been satisfied as applied to claims 67, 70, 73-81, 84-91, 96-109, and 111-179, as currently amended.

The Examiner has stated that Nagley discloses what is described above, but does not teach a particular dosage of 6 g/m<sup>2</sup> and uses the teaching of Page to cure this deficiency (see, page 5, first paragraph of the Office Action). The Examiner's position seems to be that Page reflects the general state of art pointing out to the safe and effective use of certain uridine dosing, thus providing an expectation of success one would have when treating mitochondrial disorders using the teachings of Nagley. While the Applicant agrees that Page teaches such dosages, he respectfully disagrees that Page provides any such expectation of success. In addition, the Applicant respectfully points out that the combination of Page and Nagley still fails to satisfy one of the crucial requirements of KSR, i.e., fails to teach or suggest all of the limitations recited in claims 67, 91, 111, and 129.

Indeed, as discussed above, Nagley fails to disclose or suggest any specific disease or condition recited in claims 67, 91, 111, and 129. Page likewise fails to either disclose or suggest any such diseases. Page only discusses treatment of certain disorders such as developmental delay, language deficit, behavioral problems, seizures, ataxia, and infections. It may be true that teachings of Page would create expectation of success if one intended to treat any of these disorders. However, there is no nothing in either Nagley or Page or in combination thereof showing that the method can be also successfully used for treatment of any other diseases, including those now recited in claims 67, 91, 111, and 129.

One skilled in the art would immediately realize that a successful method for treatment of certain disorders or diseases may not be, without more, adopted for treatment of other diseases, even if the two groups of diseases have something in common, like the mitochondrial nature. The Examiner has not provided any evidence showing that the methods adopted in Nagley and Page may be extrapolated to be used for treatment of any diseases listed in claims 67, 91, 111, and 129.

In view of the foregoing, it is respectfully submitted that each of claims 67, 91, 111, and 129 is patentably distinguishable over Nagley in view of Page. Each of claims 70, 73-81, 84-90, 96-109, 112-128, and 130-145 directly or indirectly depends on either claim 67, 91, 111, or 129, and is accordingly considered patentable for at least the same reason. As to claims 146-178, the rejection has become moot in view of the cancellation of claims 146-180. Withdrawal of the rejection and reconsideration are respectfully requested.

**D. Rejections Under 35 U.S.C. § 112, First and Second Paragraphs**

Claims 67, 70, 73-81, 84-90, 95-109, 111-163, and 165-179 stand rejected under 35 U.S.C. § 112, first paragraph for allegedly failing to comply with both the written description, enablement and best mode requirements (penultimate paragraph on page 5 of the Office Action). These rejections are respectfully traversed.

The Examiner stated that the limitation directed to a treatment of a mitochondrial disorder for a subject "at risk of having such disorder" as recited in claims 67, 111, and 146 lacks support in the specification. By the present amendment, the limitation has been deleted from claims 67 and 111, and claims 146-180 have been canceled altogether. Claim 129 has been also amended in the same fashion.

Accordingly, the rejection has become moot. In view of the foregoing, it is respectfully submitted that the rejection under both first and second paragraphs of 35 U.S.C. § 112 do not apply. Reconsideration and withdrawal of the rejection are respectfully requested.

In the Application of:  
Robert K. Naviaux  
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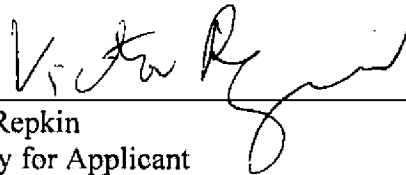
**CONCLUSION**

In view of the above amendments and remarks, reconsideration and favorable action on all claims are respectfully requested. In the event any matters remain to be resolved, the Examiner is requested to contact the undersigned at the telephone number given below so that a prompt disposition of this application can be achieved.

No fee is deemed to be due in connection with this response. However, the Commissioner is hereby authorized to charge any other fees that may be due in connection with the filing of this paper, or credit any overpayment to Deposit Account No. 07-1896, referencing the above-referenced Attorney docket number.

Respectfully submitted,

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